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Research Article

ASSOCIATION OF PREVALENCE OF COMPLICATIONS WITH DURATION OF DIABETES IN TYPE 2 DIABETICS OF JAMMU REGION

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ABSTRACT

Diabetic complications are common cause of morbidity and mortality in addition to a huge burden on healthcare system worldwide. Aim of this study was to know prevalence of various diabetic complications and their association with duration of diabetes in Type 2 diabetics of Jammu Region, winter capital of Jammu and Kashmir. Out of 200 diabetic patients selected for the study, 80 (40%) patients had not developed any complication. 120 (60%) of the patients were found to have developed one or more complications of diabetes. 46 (23%) were found to have microvascular complications, 32 (16%) macrovascular and 42 (21%) have both micro as well as macrovascular complication. It was observed, as the duration of diabetes increased the prevalence of microvascular complications increased from 1 to 15%, macrovascular complications from 1 to 7% and both micro and macrovascular complications increased from 0.5% to 10.5%. Increase in duration of diabetes leads to increase in complications.

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INTRODUCTION

Diabetes is the most challenging health problem of 21st century and has become an epidemic. It is one of the most common non communicable diseases, preventable and treatable. It is revealed by International Diabetes Federation that 1 in 11 adults will have diabetes (425 million), 1 in 2 adults is undiagnosed (212 million), 1 in 6 births is affected by hyperglycemia (or gestational diabetes), two thirds of people with diabetes are in working age group (327 millions) and 12% of global health expenditure is spent on diabetes. Prevalence of diabetes is increasing in low and middle income countries (IDF Atlas 8th Edition 2017). Diabetes mellitus is a group of common metabolic disorders that share a phenotype of hyperglycaemia. It is a chronic disease that requires long term medical attention to prevent development of devastating complications and managing them when they do occur. It is an important cause of morbidity and mortality because of prolonged chronic hyperglycemia, with altered glucose homeostasis during silent course of the disease which lead to

diffuse endothelial damage responsible for various chronic complications of the diabetes (Faucy et al, 2015).

Diabetes is common cause of hospitalisations because of its acute and chronic complications. Acute complications of diabetes are ketoacidosis, hyperosmolar hyperglycaemic state and hypoglycaemia. Various chronic complications of diabetes are macrovascular complications like coronary artery disease (CAD), peripheral vascular disease (PVD), cerebrovascular disease (CVD) and microvascular complications are retinopathy, neuropathy and nephropathy. Uncontrolled hyperglycemia has deleterious effects as it causes endothelial damage that cause changes in multiple organs systems leading to failure of those organs (Faucy et al, 2015). Chronic macrovascular and microvascular complications of diabetes lead to various disabilities like lower limb amputations, stroke, retinopathy leading to blindness and nephropathy leading to end stage renal disease (ESRD). ESRD requires either renal replacement therapy or lifelong dialysis. Uncontrolled diabetes and its complications impose a tremendous burden on the economy of individual, his family and the nation due to loss of

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work and wages. Complications of diabetes mellitus cause various disabilities, reduce quality of life and are responsible for morbidity and premature mortality (Murray and Lopez, 2013).

It has been reported that prevalence of diabetic complications is neuropathy 42.6%, cardiovascular diseases 23.6%, nephropathy 21.1%, retinopathy 16.6% and foot ulcers 5.5% (Mohan et al, 2013). In another study from Tamil Nadu prevalence of diabetic complications reported is CVD 7.8%, stroke 0.5%, nephropathy 30.7%, neuropathy 59% and retinopathy 32.8% (Maniarasu and Muthunaryan, 2017). Prevalence of diabetes type 2 in Jammu Region, winter capital of Jammu and Kashmir is 8.1% (Jallu et al, 2015). There is no study regarding prevalence of diabetic complications from Jammu. Poor glycemic control, genetic histoty and prolonged duration of diabetes are most important factors for development of various complications and ethnic variability in the susceptibility to the complications might also exist. Keeping in view the prevalence of diabetic complications the present study was planned to investigate the prevalence of complications in individuals suffering from diabetes and association with duration of diabetes.

MATERIALS AND METHODS

This was a cross sectional study and was conducted in the department of Biochemistry in collaboration with department of Medicine, Acharya Shri Chander college Of Medical Sciences (ASCOMS) and Hospital Sidhra, Jammu. 200 type 2 known diabetics with and without complications of diabetes, were recruited for the study. The study was approved by ethics committee of ASCOMS and hospital. Informed consent for the inclusion of the patient in study was taken from him or her and the purpose of the study was indicated clearly to the participating individuals in vernacular language. Patients suffering from other diseases like thyroid dysfunction, any type of malignancy, Alzheimer's and Asthmatics were not included. Patients on cyclosporins and steroid immunosuppressant were also excluded from study. The detailed history about duration of diabetes, hypertension, their dietary habits, life style, smoking habits and presence of any complication of diabetes was noted as per the Performa designed. Presence of complications was noted from medical records of patients.

All the patients were advised to observe an overnight fast and to comply with the instructions. Blood and urine samples were collected early in the morning. About six ml of blood was collected by venepuncture of the ante-cubital vein. The blood sample was divided into three vials, one containing anticoagulant (sodium fluoride and potassium oxalate) for plasma separation for estimation of blood glucose, in plain vials for serum separation and a vial containing EDTA for Glycated haemoglobin (HbA1c).

Fasting blood glucose was estimated by enzymatic GOD/POD Method (Trinder, 1969), Blood Urea was estimated by GLDH-Urease method (Tiffany et al, 1972), Serum creatinine was estimated Jaffes Alkaline Picrate Method (Bowers, 1980), Glycated hemoglobin was estimated by ion exchange chromatography (Nathan et al, 1984) Microalbumin in urine was estimated by Pyrogallol Red method (Phllpou et al, 1989), Serum Cystatin-C was estimated by automated immunoassay (Newman et al, 1995). Microalbumin in urine was estimated by

Pyrogallol Red method (Phllpou et al, 1989). Serum total cholesterol will be estimated by enzymatic (CHOD-PAP method of Allain CC 1974). Serum HDL was estimated by the autozyme precipitation reagent method in conjunction with autozyme cholesterol reagent – for enzymatic determination of HDL cholesterol in the supernatant (Burstein et al, 1970). Serum LDL-C was calculated (by Friedwald's formula 1972). Serum triglyceride was estimated by enzymatic method (Trinder, 1968). Serum electrolytes sodium and potassium were analyzed with ion selective electrodes (Levy, 1981). Serum calcium was estimated by Orthocresolphthalein method (Harold et al, 1966). Comparison of means of various biochemical parameters was done using student t test. Analysis of variance (ANOVA) was applied for comparison between groups.

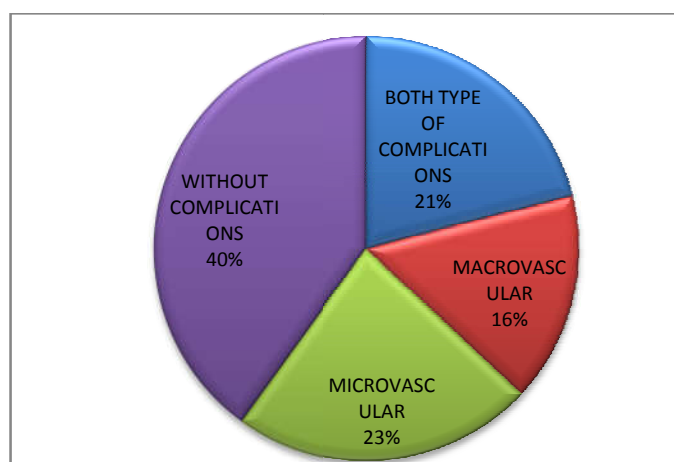


Figure 1 Prevalence of different complications in Type 2 diabetics of Jammu Region.

Table I Diabetic Patients with and without complications

Duration of diabetes	Total no of Patients	Diabetics without complications	Diabetics with complications
≤5 years	15(7.5%)	10(5%)	5(2.5%)
>5-10 years	93(46.5%)	43(21.5%)	50(25%)
>10 years	92(46%)	27(13.5%)	65(32.5%)

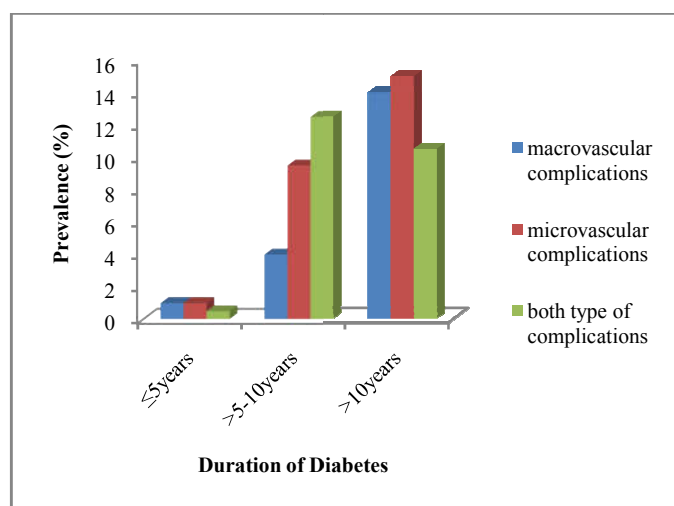


Figure 2 Prevalence of different types of complications in Diabetes

Table II Prevalence of macrovascular and microvascular complications

Duration of diabetes	CAD	PAD	CVD	Retinopathy	Neuropathy	Nephropathy
≤5years	4 (2%)	0 (0%)	1 (0.5%)	2 (1%)	1 (0.5%)	3(1.5%)
>5-10 yrs	20(10%)	6(3 %)	3 (1.5%)	13 (6.5%)	12 (6%)	20(10%)
>10years	21(10.5%)	6(3%)	9 (4.5%)	18 (9%)	17 (8.5%)	41(20.5%)

Table III Baseline metabolic parameters of patients and duration of diabetes

Parameters	Duration of diabetes			P value
	≤5 years	>5-10 years	>10 years	
HbA1c (%)	7.7±1.2	7.3±1.1	8.0±1.2	0.001
Blood Glucose (mg/dl)	229±109	159±97	178±90	0.001
Urea (mg/dl)	44±34	43±24	63±48	0.002
Creatinine (mg/dl)	1.6±1.6	1.4±0.9	1.3±1.3	0.254
Cystatin-C (mg/L)	1.4±0.8	1.6±0.7	1.4±0.9	0.002
Microprotein (mg/day)	163±29	368±248	369±353	0.421
Cholesterol (mg/dl)	188±55	192±43	187±43	0.632
Triglyceride (mg/dl)	184±60	176±50	178±51	0.786
HDL-C (mg/dl)	32±5	41±7	26±8	0.35
LDL-C (mg/dl)	106±56	113±42	111±39	0.83
VLDL-C (mg/dl)	21±12	22±14	57±18	0.65
Total Plasma Proteins (g/dl)	7.4±0.7	6.8±0.7	6.9±0.8	0.54
Albumin (g/dl)	3.6±1.1	3.8±0.9	3.4±1.0	0.31
Sodium (mmol/L)	134±3.6	136±3.8	138±3.8	0.12
Potassium (mmol/L)	4.0±3.6	4.1±0.5	4.2±0.7	0.51
Calcium (mg/dl)	8.9±1.3	9.1±1.3	8.7±1.2	0.35

RESULTS

200 type 2 diabetic patients were randomly selected from amongst the individual of Jammu population visiting Acharya Shri Chander College of Medical Sciences (ASCOMS) and Hospital Sidhra Jammu. Out of 200 patients involved in the study 119 (59.5%) were males with an average age of 57± years and 81(40.5%) were females with an average age of 55±9 years. Out of 200 patients 120 (60%) suffered complications whereas 80 (40%) patients had not developed any complications. Out of 120 individuals 51 (25.5 %) suffered from microvascular complications and 24 (12 %) suffered from macrovascular complications and 45 (22.5%) had both microvascular as well as macrovascular complications (Fig 1).

All the individuals were divided into 3 groups depending upon duration of diabetes. When duration of diabetes is ≤5 years, out of 15(7.5%) individuals, 10(5%) had no complications whereas 5(2.5%) had begin with diabetic complications. Out of 5, 1(0.5%) suffered both macrovascular and microvascular complications, 2(1%) macrovascular complications and 2(1%) suffered microvascular complications (Table 1 and Fig 2).

When duration of diabetes is >5-10 years out of 93(46.5%), 43(21.5%) individuals had not developed any complication and 50(25%) individuals suffered complications. Out of 50, 23(11.5%) individuals suffered both macrovascular and microvascular complications, 8(4%) macrovascular complications and 19(9.5%) suffered microvascular complications. When duration of diabetes was >10 years, out of 92 (46%) individuals, 27 (13.5%) individuals had not suffered any complications and 65(32.5%) had developed complications (Table 1 and Fig 2).

When duration of diabetes is ≤5 years, among microvascular complications 3(1.5%) individuals suffered nephropathy, 2(1%) individuals suffered retinopathy, 1(0.5%) neuropathy. Among macrovascular complications 4(2%) individuals

suffered CAD, 1(0.5%) individuals suffered CVD and no individual suffered peripheral arterial disease. When duration of diabetes is >5-10 years, number of individuals suffering from microvascular complications increased to, 13(6.5%) retinopathy, 12(6%) neuropathy, 20(10%) nephropathy. Number of individuals suffering from macrovascular complications also increased, CAD, 20(10%), PAD 6(3%) and CVD 3(1.5%). When duration of diabetes is >10 years number of individuals suffering from microvascular complications increased retinopathy 18(9%), neuropathy 17(8.5%) and nephropathy 41(20.5%). Macrovascular complications like CAD and PAD increased to 21(10.5%) and 6 (3%) respectively whereas number of patients suffering from CVD increased to 9 (4.5%) (Table 2). Prevalence of both type of complications increased with increasing duration of diabetes. Blood levels of various biochemical parameters like glucose, urea, HbA1c and Cystatin-c increased significantly with increasing duration of diabetes (P<0.05) (Table 3).

Frequency of proteinuria noted in patients was normoalbuminuria 92 (46%), microalbuminuria 72 (36%) and macroalbuminuria 36 (18%).Complications were more common in females as compared to males. A positive Family history of diabetes was seen in 64 (32%) individuals.74 (37%) individuals had BMI > 25 kg/m², 136 (68%) patients had hypertension. Dislipidemia was seen in 70 (35%) patients.

DISCUSSION

Diabetes is associated with severe impact on quality of life due to development of various chronic complications. It forces patients to live quality compromised life years or disability adjusted life years due to various disabilities like blindness, lower limb amputation and stroke. Management and treatment of diabetes and its associated complications imposes huge financial burden on patient, family and also on economy of a nation. As per IDF estimates in 2017 India has 10.4% of adult population of diabetes with an equal number of undiagnosed patients and are at increased risk for developing diabetic complications. In 2016 approximately 1 million deaths occurred in India. More than half of these deaths (53.2%) occurred in people in working age group due to complications of diabetes.

In our study two third patients were suffering from at least one complication. Among microvascular complications prevalence of retinopathy is 16.5%, same figures were reported from South India (Mohan *et al*, 2013). This prevalence is lower than another study 30% reported from Madhya Pradesh (Jain *et al*, 2016). Our study shows that 32% patients are suffering from nephropathy consistent with study at Chennai (CUPS no 5), higher than reported from China 29.3% (Jia *et al*, 2009) little higher than a study from Tamil Nadu 30.7% (Karthikeyan Manirasu, Logaraj Muthunayanan 2017) and much higher than global prevalence of CKD which is 22% as reported by IDF (8th edition 2017). Prevalence of end stage renal diseases is up to 10 times higher in people with diabetes. Prevalence of neuropathy was 15%, consistent with a study from Goa (Vaz *et al*, 2011). Prevalence of CAD is 22.5% almost consistent to a study done in Chennai which revealed a prevalence of 21.4% (Mohan *et al*, 2001) and higher than which reported a prevalence of 16.2% (Krishan, 2012). Diabetes is characterised by hyperglycemia, dislipidemia and insulin resistance. These

pathological states are responsible for development and progression of peripheral vascular disease through mechanisms similar to CAD. These mechanisms are inflammation, endothelial dysfunction; plateletlet dysfunction and hypercoagulation that accelerate atherosclerosis and atherothrombosis. PVD is a major risk for nontraumatic lower limb amputations. As per IDF 2017 every 30 seconds a lower limb or a part of lower limb is lost to amputation somewhere in world as consequence of diabetes. Early diagnosis and appropriate management can prevent amputation and reduce morbidity and mortality. Prevalence of PAD in our study is 6% which is lower than reported in a study from South India 7.8% (Premalatha et al, 2000) and another study reported a prevalence of 14.3% (Aggarwal et al, 2012). Prevalence of cerebrovascular diseases in our study is 6.5%, consistent with a study from Saudi Arabia (Aboud et al, 2016) and higher than another study which reported a prevalence of 3.5% (Fatma Al-Maskari, Mohammed El Sadiq and John N Norman 2007). Prevalence of all complications is increasing with duration of diabetes. The changes in levels of blood glucose, urea, HbA1c and Cystatin –C were statistically significant (p value<0.05) with increasing duration of the disease whereas other biochemical parameters didn't show any statistically significant variation with increasing duration of the disease (Table 3).

CONCLUSION

As prevalence of diabetic complications is increasing with duration of diabetes there is an urgent need to slow down epidemic of diabetes to reduce the burden of various associated complications. We propose early aggressive screening of various complications, appropriate measures to prevent or retard the development and progression of these complications. Several risk factors are implicated in pathogenesis of diabetic complications which are modifiable and non modifiable. Non modifiable are duration of diabetes, age at onset, genetic history and ethnicity. Duration is a non modifiable risk factor but keeping a control on modifiable risk factors such as hyperglycemia, hypertension, dislipidemia, high BMI, smoking can prevent or delay the development and progression of various complications. So patient education regarding adoption of low glycemic high fibre diet, good exercise, compliance to treatment for control of hyperglycemia, hypertension and lipids will reduce the morbidity and mortality because of diabetes associated complications and economic burden on individuals as well as healthcare system.

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